UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/446,711 | 04/03/2000 | FRANCE ALLARD | P04334US00 | 2785 |

7590 09/23/2003

HEIDI S NEBEL
ZARLEY MCKEE THOMTE VOORHEES & SEASE
801 GRAND AVENUE
SUITE 3200
DES MOINES, IA 50309-2721

| EXAMINER | |
|---|---|
| COLLINS, CYNTHIA E | |
| ART UNIT | PAPER NUMBER |
| 1638 | 22 |

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/446,711 | ALLARD ET AL. | |
| | Examiner | Art Unit | |
| | Cynthia Collins | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4,9-14,16-22,24,38 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-14,16-22,24,38 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 2, 2003 has been entered.

Claims 5-8, 15, 23 and 25-37 are cancelled.

Claims 1, 4 and 22 are currently amended.

Claims 1-4, 9-14, 16-22, 24 and 38-39 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Drawings*

Applicant's petition to accept color photographs filed under 37 CFR 1.84(a)(2) is acknowledged.

### *Claim Objections*

Claim 10 is objected to because of the following informalities: the claim ends in two periods. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

Claim 4 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth for claims 4-6 in the office action mailed August 13, 2002.

Applicant's arguments filed July 2, 2003, have been fully considered but they are not persuasive.

Applicant argues that the invention is enabled in light of the amendment of claim 4 to limit the method to a gramineae species plant. Applicant reiterates that support and evidence for the overexpression of betaine dehydrogenase and choline monooxygenase was set forth in their previous response, and that one skilled in the art would have been familiar with the techniques necessary for expressing such genes at the time of filing. Applicant additionally argues that the description clearly teaches that increasing the betaine concentration in a plant results in an increase in cold or freezing tolerance of the plant (reply page 3).

The Examiner continues to maintain that the mere assertion in the specification that overexpressing betaine dehydrogenase and choline monooxygenase under a low temperature-induced promoter may allow the accumulation of betaine does not enable the claimed invention, because overexpressing betaine dehydrogenase or choline monooxygenase in a plant in a manner that results in accumulation of betaine sufficient to affect cold or freezing tolerance is unpredictable.

The Examiner additionally maintains that overexpressing betaine dehydrogenase and/or choline monooxygenase in a plant in a manner that results in an increase in the concentration of betaine that is non-toxic is unpredictable, as the amount of betaine that would accumulate in a transgenic plant would be dependent on a number of variables, including but not limited to the level and location and timing of expression of the enzyme(s), the stability of the enzyme(s), the level of enzymatic activity, the availability of substrate(s), and the availability and activity of subsequent enzymes in the biosynthetic pathway. Neither the specification nor the prior art provide guidance with respect to how to express betaine dehydrogenase and/or choline monooxygenase in a gramineae species plant in a manner that results in an increase in the concentration of betaine that is non-toxic. Absent such guidance, it would require trial and error experimentation for one skilled in the art to determine which betaine dehydrogenase and/or choline monooxygenase gene to express, and how to express it/them, a gramineae species plant, in a manner that results in an increase in the concentration of betaine that is non-toxic.

The Examiner further maintains that combining cold acclimation with the overexpression of betaine dehydrogenase and/or choline monooxygenase in a plant in a manner that results in increased or induced cold or freezing tolerance of a plant over and above that of the normal genotypic potential is unpredictable, because, for the reasons just stated, the amount of betaine that would accumulate in a transgenic plant overexpressing betaine dehydrogenase and/or choline monooxygenase is unpredictable. Neither the specification nor the prior art provide guidance with respect to how to express betaine dehydrogenase and/or choline monooxygenase a gramineae species plant in a manner that results in an increase in the concentration of betaine that, when combined with cold acclimation, would result in increased or induced cold or freezing

tolerance of a plant over and above that of the normal genotypic potential. Absent such guidance, it would require trial and error experimentation for one skilled in the art to determine which betaine dehydrogenase and/or choline monooxygenase gene to express, and how to express it/them, a gramineae species plant, in a manner that, when combined with cold acclimation, would result in increased or induced cold or freezing tolerance of a plant over and above that of the normal genotypic potential.

The Examiner also continues to maintain that she does not generally question the enablement of the specific methods for increasing the concentration of glycine betaine by metabolic engineering disclosed in the post-filing date art, or the general proposition that increasing the betaine concentration in a plant can result in an increase in cold or freezing tolerance of the plant. The Examiner continues to maintain, however, that Applicant is not enabled for the claimed method, because Applicant has not disclosed any method for increasing the concentration of glycine betaine by metabolic engineering, and because neither Applicant nor the prior art disclose any method for increasing or inducing cold or freezing tolerance of any gramineae plant species over and above that of its normal genotypic potential by combining cold acclimation with increasing the concentration of glycine betaine by metabolic engineering.

Claims 1-3, 9-14, 16-22, 24 and 38-39 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing or inducing cold or freezing tolerance in the wheat cultivar Glenlea, said method comprising simultaneously acclimating the plant and increasing the concentration of betaine in the plant by administering a betaine composition, wherein the lethal temperature of the plant is decreased,

wherein the acclimation temperature is 6° C during the day and 2° C during the night, and wherein the betaine composition comprises betaine at 100 to 250 mM, does not reasonably provide enablement for other methods of increasing or inducing cold or freezing tolerance in other plants, for the reasons of record set forth in the office action mailed August 13, 2002.

Applicant's reply filed July 2, 2003, does not address the prior rejection of claims 1-3, 9-14, 16-22, 24, 36 and 38-39 under 35 U.S.C. 112, first paragraph, for scope of enablement. Accordingly, the rejection is maintained.

Claim 1, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Part a) of claim 1 requires acclimating a plant, but the claim sets forth no steps by which this may be accomplished. Additionally, part b) of claim 1 requires increasing the concentration of betaine or a derivative thereof in a plant, but the claim sets forth no steps by which this may be accomplished.

Claims 24 and 38-39, and claims dependent thereon, remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "gramineae species" and "grasses", for the reasons of record set forth in the office action mailed August 13, 2002.

Applicant's arguments filed July 2, 2003, have been fully considered but they are not persuasive.

Applicant argues that the amendment of the claims to delete reference to "grass plant" should overcome the rejection (reply page 12).

The rejection is maintained because claims 24 and 38-39 continue to refer to "gramineae species" and "grasses". It is unclear what is intended by "grasses" in this context, as "gramineae species" would ordinarily be considered to include "grasses".

Claims 24 and 38-39, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "grasses". There is insufficient antecedent basis for "grasses" in claim 1 from which claims 24 and 38-39 depend.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 9, 12-14, 16, 18, 22, 24 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Rajashekar et al. (Plant Physiology, 1996, Vol. 111, No. 2 SUPPL., page 70).

The claims are drawn to a method of increasing or inducing cold or freezing tolerance in rosaceae or gramineae plants, including strawberry plants, by acclimating the plants and increasing the concentration of betaine or a derivative thereof, including glycine betaine, in said plant by administering to said plant betaine or a derivative thereof, including betaine or a derivative thereof at a concentration lower than about 500 nM.

Rajashekar et al. teach a method of inducing cold tolerance in cold-hardening strawberry plants by applying glycine betaine at a concentration of 2mM. While Rajashekar et al. do not

explicitly teach that their method induces cold tolerance over and above that of the normal genotypic potential induced by each step alone, the method taught by Rajashekar et al. must necessarily produce such a result, since the method taught by Rajashekar et al. includes all the affirmative method steps set forth in the rejected claims. Likewise, while Rajashekar et al. do not explicitly teach that their method decreases the lethal temperature of the plant, or that their method increases freezing tolerance by at least 6°C, or that their method further results in improving regrowth, greening and resistance to photoinhibition, the method taught by Rajashekar et al. must necessarily produce such results, since the method taught by Rajashekar et al. includes all the affirmative method steps set forth in the rejected claims.

***Claim Rejections - 35 USC § 103***

Claims 10-11, 17, 21 and 39 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rajashekar et al. (Plant Physiology, 1996, Vol. 111, No. 2 SUPPL., page 70) in view of Kishitani et al. (Plant, Cell, and Environment, 1994, Vol. 17, pages 89-95), and in light of Zhao et al. (Journal of Plant Physiology, 1992, Vol. 140, pages 541-543), for the reasons of record set forth in the office action mailed August 13, 2002.

Applicant's arguments filed July 2, 2003, have been fully considered but they are not persuasive.

Applicant argues that the rejection is contradictory to the assertion that the full scope of the invention is not enabled because the effect of betaine accumulation in plants is unpredictable. Applicant also argues that one could not predict the dramatic results of combining betaines and cold acclimation from the combined references. Applicant further argues that there is no support

for the Examiner's position that increased freezing or cold tolerance at the leaf level is indicative of a significant increase at the whole plant level, and points out that in certain cases leaves may show significant resistance to freezing while roots do not. Applicant argues that the claimed invention is commensurate in scope with the teachings disclosed specification, and that the rejected claims are enabled and are not obvious in view of the prior art. Applicant specifically points to the results set forth in the disclosure for wheat, which demonstrate a significant synergistic effect when cold acclimation and betaine application are combined. Applicant also points out that the disclosed mechanistic of action of this synergism were not know in the art prior to applicant's invention (reply pages 9-11).

The rejection is not contradictory to the assertion that the full scope of the invention is not enabled because the effect of betaine accumulation in plants is unpredictable. Whether the specification provides sufficient guidance for practicing the full scope of the claimed and whether the claimed invention is obvious in light of the prior art are separate issues. At the time of filing it was known that cold tolerance could be induced in strawberry plants by acclimating the plants and by administering exogenous glycine betaine. At the time of filing it was also known that glycine betaine accumulates in plants during cold acclimation, that glycine betaine levels in plants correlates with freezing tolerance, and that exogenously applied glycine betaine can act as a cryoprotectant in plants. The rejected claims recite no limitations that distinguish what is claimed from what was already known in the art.

With respect to Applicant's assertion that that one could not predict the dramatic results of combining betaines and cold acclimation from the combined references, the Examiner maintains that the assertion is not commensurate in scope with the rejected claims. The Examiner

acknowledges the results set forth in the disclosure for wheat, but maintains that the rejected claims are obvious because they are not limited to the exemplified method which demonstrates a significant synergistic effect when cold acclimation and betaine application are combined. The rejected claims are directed to methods of increasing or inducing any level of cold or freezing tolerance in rosaceae or graminae plants by acclimating said plants and increasing the betaine concentration to any level that is nontoxic. The Examiner further maintains that the failure of the prior art to teach the mechanistic of action of the synergism of acclimation and betaine accumulation does not render the claimed invention nonobvious, as the correlation between betaine accumulation and cold tolerance was well established in the art at the time of filing.

With respect to the argument that there is no support for the Examiner's position that increased freezing or cold tolerance at the leaf level is indicative of a significant increase at the whole plant level, the Examiner maintains that increased freezing or cold tolerance at the leaf level is indicative of a significant increase at the whole plant level, as the prior art of Rajashekar et al. teaches the induction of cold tolerance upon the application of glycine betaine to "cold hardening plants". Since glycine betaine was applied to whole cold-hardening plants, increased freezing or cold tolerance of any plant part assayed would be indicative of a significant increase at the whole plant level, as all plant parts appear to have been subject to the both acclimation and betaine application. Furthermore, the claims make no distinction with respect to the induced cold or freezing tolerance being limited to any particular plant part, or as having to be assayed at the whole plant level.

***Remarks***

No claim is allowed.

Claims 4 and 19-20 are deemed free of the prior art due to the failure of the prior art to teach or suggest a method of increasing or inducing cold or freezing tolerance in rosaceae or graminae species plants by acclimating a plant and increasing the concentration of betaine by overexpressing a betaine dehydrogenase and/or choline monooxygenase gene, or a method of increasing or inducing cold or freezing tolerance in graminae species plants by acclimating a plant and increasing the concentration of betaine or a derivative thereof at a concentration of about 250 mM.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
September 15, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638